37

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/978,423	10/16/2001	Avi J. Ashkenazi	GNE.2630P1C21	5291

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EXAMINER	
LE, EMILY M	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 02/07/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/978,423	ASHKENAZI ET AL.	
	Examiner	Art Unit	
	Emily Le	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09/28/2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *58-62* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *58-62* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *09/28/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 09/28/2005 has been entered.

Status of Claims

2. Claims 1-57 and 63 are cancelled. Claims 58-62 are pending and under examination.

Correction of Inventorship

3. The request for the deletion of inventors in this nonprovisional application under 37 CFR 1.48(b) is **granted**.

The following inventors are deleted:

Avi J. Ashkenazi	Kevin P. Baker
David Botstein	Luc Desnoyers
Dan L. Eaton	Napoleone Ferrara
Ellen Filvaroff	Sherman Fong
Wei-Qiang Gao	Hanspeter Gerber
Mary E. Gerritsen	J. Christopher Grimaldi
Kenneth J. Hillan	Ivar J. Kljavin
Sophia S. Kuo	Mary A. Napier
James Pan	Nicholas F. Paoni
Margaret Roy	Timothy A. Stewart
Daniel Tumas	P. Mickey Williams

The correct inventors are: Audrey Goddard, Paul Godowski, Austin Gurney, David Shelton and William Wood.

Information Disclosure Statement

4. Previously: The information disclosure statement filed 04/11/2005, Supplemental Information Disclosure Statement Under 37 C.F.R § 1.97 fails to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because the filling is incomplete. The statement filed is not accompanied with a listing of the document(s) on a PTO-1449, as set forth in 37 C.F.R § 1.98. It has been placed in the application file, but the information referred to therein has not been considered as to the merits. Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609 ¶ C(1).

In response, Applicant requests the Examiner to consider the filed IDS, and states that the IDS is accordance with 37 C.F.R. 1.97(c) and that PTO 1449 is not required.

Applicant is correct to note that the filed IDS is in compliance with 37 C.F.R 1.97 (c), and that citation of the reference on a PTO 1449 is not required. However, what is required is compliance with the requirement(s) set forth in 37 C.F.R 1.98. 37 C.F.R 1.98 states:

(a) Any information disclosure statement filed under § 1.97 shall include the items listed in paragraphs (a)(1), (a)(2) and (a)(3) of this section.

(1) A list of all patents, publications, applications, or other information submitted for consideration by the Office. U.S. patents and U.S. patent application publications must be listed in a section separately from citations of other documents. Each page of the list must include:

(i) The application number of the application in which the information disclosure statement is being submitted;

(ii) A column that provides a space, next to each document to be considered, for the examiner's initials; and

(iii) A heading that clearly indicates that the list is an information disclosure statement.

(2) A legible copy of:

(i) Each foreign patent;

(ii) Each publication or that portion which caused it to be listed, other than U.S. patents and U.S. patent application publications unless required by the Office;

(iii) For each cited pending unpublished U.S. application, the application specification including the claims, and any drawing of the application, or that portion of the application which caused it to be listed including any claims directed to that portion; and

(iv) All other information or that portion which caused it to be listed.

(3) (i) A concise explanation of the relevance, as it is presently understood by the individual designated in § 1.56(c) most knowledgeable about the content of the information, of each patent, publication, or other information listed that is not in the English language. The concise explanation may be either separate from applicant's specification or incorporated therein.

(3) (ii) A copy of the translation if a written English-language translation of non-English-language document, or portion thereof, is within the possession, custody, or control of, or is readily available to any individual designated in § 1.56(c).

5. The information disclosure statement (IDS) submitted 09/28/2005 has been considered by the Examiner. However, since the Blast results cited therein are not true publications with a publication date, they are not fully in compliance with 37 CFR 1.97 and thus they will not be printed on the face of the patent issuing from this application.

Claim Rejections - 35 USC § 101

6. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

7. The utility rejection is hereby withdrawn in view of Applicant's 09/28/2005 submission, pages 6-11. In the cited passages, Applicant convincingly submits that the claimed polypeptide, an allele or isoforms having 95.9% identity to neuroligin 4, can be use to treat conditions where transmission of a signal is not desired, such as pain.

Priority

8. In view of Applicant's 09/28/2005 submission, pages 11-12, the claimed invention is granted the priority date of 04/01/1998.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 58-62 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to

one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are directed to an antibody that binds to SEQ ID NO: 375.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient description of a representative number of species by i) actual reduction to practice, ii) reduction to drawings, or iii) disclosure of relevant identifying characteristics. Examples of factors to be considered for the latter requirement include:

- disclosure of complete or partial structure,
- physical and/or chemical properties,
- functional characteristics,
- correlation between structure and function, and
- methods of making.

Each of the listed criteria is addressed in turn below.

i) sufficient description of a representative number of species by actual reduction to practice: The specification only provides generic teachings of how to make antibodies; however, no evidence can be ascertained from the specification suggesting that Applicant has made the claimed antibody.

ii) sufficient description of a representative number of species by reduction to drawings: The drawings do not contain a description of the claimed antibody.

iii) sufficient description of a representative number of species by disclosure of relevant identifying characteristics:

- disclosure of complete or partial structure: Complete or partial structures of the claimed antibody cannot be found in the specification. The specification also fail to provide any guidance pertaining to the structural requirements modulating antigen-antibody binding. For instances, which amino acids in the complementary region (CDR) are essential for antibody binding?
- physical and/or chemical properties: The disclosure fails to provide any guidance pertaining to the physical and/or chemical properties of the antibody. For instance, the speciation is silent pertaining to antibody class, the binding affinity, avidity and specificity.
- correlation between structure and function: The specification fails to identify the molecular determinants modulating antigen-antibody binding. The disclosure fails to identify any epitopes recognized by the claimed antibody. The disclosure also fail to provide any guidance pertaining toe the amino acid in the CDR region that are required for binding. In the absence of such guidance, a correlation between the required binding activity and a structure cannot be ascertained.

The issue here is not whether the skilled artisan would be able to make the claimed antibody; but whether or not the Applicant was in **possession** of the claimed invention at the time of filing. A review of the specification shows that Applicant clearly has not made the claimed antibody. In the instant, all that is provided in the specification are generic teachings directed at the employment of various known techniques to make

antibodies; however, that is all that is disclosed in the specification. The specification does not contain any evidence suggesting and/or showing that the claimed antibody, one that binds to SEQ ID NO: 375, was made by Applicant. There is no evidence provided in the specification to suggest SEQ ID NO: 375 was ever immunized to an animal to obtain the desired antibody. There is no evidence provided int eh specification that suggests or demonstrates that Applicant isolated and purified the protein corresponding to SEQ ID NO: 375. There is no evidence to suggest that the protein was combined with an adjuvant or carrier and included in an immunogenic composition. There is no evidence to suggest that said composition was administered to a host and the resultant antibodies were isolated and characterized. Without any evidence suggesting that the claimed antibody was ever made, it is evident that Applicant was not in possession of the claimed antibody at the time the invention is filed.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the disclosure lacks evidence suggesting or showing that the claimed antibody was ever in Applicant's possession at the time of filing. And therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or

simplicity of the method of making antibodies. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating/making it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

Therefore, the full breadth of the claims fails to meet the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. The rejection under 35 U.S.C. 102(b) is withdrawn in view of Applicant's submission.

In response to the rejection set forth in the previous office action, Applicant amends the claims to recite an isolated antibody that specifically binds to SEQ ID NO: 375.

It is noted that Applicant defines an antibody that "specifically binds" to a particular polypeptide or an epitope on a particular polypeptide as one that binds to that particular polypeptide or epitope on a particular polypeptide without substantially binding to any other polypeptide or polypeptide epitope. (Page 30 of the specification)

In view of this definition, the prior art no longer anticipates the claimed invention. It is noted that the antibody of the prior art also binds to other neuroligins, as evidenced by Ichtchenko et al., 1996 (Ichtchenko et al. Structures, alternative splicing, and neurexins binding of multiple neuroligins. The Journal of Biological Chemistry, 1996, Vol. 271, No. 5, 2676-2682.). Ichtchenko et al., 1996, teaches the antibody of Ichtchenko et al. also binds to neuroligins 2 and 3. [Figure 4 of Ichtchenko et al., 1996] Thus, the antibody of Ichtchenko et al. would not bind to SEQ ID NO: 375 with specificity. Ergo, the rejection is withdrawn.

Conclusion

13. No claims are allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Emily Le whose telephone number is (571) 272 0903. The examiner can normally be reached on Monday - Friday, 8 am - 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on (571) 272-0902. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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